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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WEDDINGTON, KEVIN E	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 02/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/669,251	SHAPIRO, LELAND	
	Examiner	Art Unit	
	Kevin E. Weddington	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 September 2003* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2-8-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 25-30 are presented for examination.

Applicants' preliminary amendment and drawings filed September 25, 2005; and the information disclosure statement filed February 8, 2005 have been received and entered.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 25 and 28 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 34-36 of copending Application No. 10/427,929. Although the conflicting claims are not identical, they are not patentably distinct from each other because present application teaches a method of treating ischemia reperfusion injury, comprising administering at least one of α1-antitrypsin-like agent (AAT); and the copending

application teaches a method of treating an animal suffering from a pathological conditions, comprising administering to the animal a therapeutically effective amount of a composition comprising at least one agent where the agent (a) suppresses nitric oxide synthesis and (b) exhibits mammalian α1-antityrpsin, α1-antitrypsin-like, elastase-inhibitory, or proteinase-3-inhibitory activity. Clearly, the copending application treats pathological conditions broadly with the said instant active ingredients, and the present application is encompassed by the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 25 and 28 are not allowed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating septic shock, induced inflammation and endotoxemia with the administration of (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl-2-(S)-methylpropyl]-L-prolinamide, does not reasonably provide enablement for treating ischemia reperfusion injury; the additional administration of a thrombolytic agent, and the additional use of a

mechanical device to reestablish blood flow. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per factors indicated in the decision In re Wands, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation.

The factors include:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice that instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to a method of treating ischemia reperfusion injury, comprising administering at least one of α1-antitrypsin, α1-antitrypsin-like agent, antielastase, or antiproteinase-3 agent, or a serine protease inhibitor, or a combination thereof; additionally comprising administering a thrombolytic agent and additionally comprising using a mechanical device to reestablish blood flow.

The relative skill of those in the art is generally that of a Ph.D. or M.D.

The present invention is unpredictable unless experimentation is shown for the treat of ischemia reperfusion injury with all the compounds of claim 1, along with all thrombolytic agents, and all mechanical device for reestablishing blood flow

The breadth of the claims

The claims are very broad and inclusive to all α1-antitrypsins, α1-antitrypsin-like agents, antielastase, or antiproteinase-3 agents, or serine protease inhibitors, or combinations thereof; all thrombolytic agents and all mechanical devices for reestablishing blood flow.

The amount of direction or guidance provided and the presence or absence of working examples

The working examples are limited to the administration of (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl-2-(S)-methylpropyl]-L-prolinamide to treat septic shock (Example 6.7), combined with γ-IFN (Example 6.8), to treating induced inflammation (Example 6.9) and combined with α1-antitrypsin to treat endotoxemia (Example 6.10).

No working examples showing the (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl-2-(S)-methylpropyl]-L-prolinamide to treat ischemia reperfusion injury.

No working examples showings the addition of a thrombolytic agent of claim 26, or the using of a mechanical device for reestablishing blood flow of claims 27 and 30.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to how the other compounds of claim 1 are effective in treating ischemia reperfusion injury or how (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl-2-(S)-methylpropyl]-L-prolinamide can treat ischemia reperfusion injury; or combined with a thrombolytic agent and a mechanical device for reestablishing blood flow. Therefore, undue experimentation would be required to practice the invention as it is claimed in its current scope.

Claims 25-30 are not allowed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 25 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Gyorkos et al. (5,618,792) of PTO-1449.

Gyorkos et al. teach substituted oxadiazole, thiadiazole and triazole peptoids, which are useful as inhibitors of serine proteases including human neutrophil elastase (elastase inhibitory activity). Note the examples I-XVI are the same compounds of disclosed in applicants' claim 1. Note particularly column 7, lines 58-67 and column 8, lines 1-67 teaches the instant compounds are formulated into pharmaceutical compositions . Column 7, lines 45-57 teaches the instant compounds are used to treat various diseases such as ischemia/reperfusion or other conditions disclosed in column 1, lines 28-42. Clearly, the cited reference anticipates the applicants' instant invention, therefore, the instant invention is unpatentable.

Claims 25 and 28 are not allowed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 25-28 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gyorkos et al. (5,618,792) in view of Verstraete, "Intravenous administration of a thrombolytic agent is the only realistic therapeutic approach in evolving myocardial infarction", European Heart Journal, Vol. 6, pp. 586-593 (1985) and further in view of Woods (5,180,366).

Gyorkos et al. were discussed above supra for the use of (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl-2-(S)-methylpropyl]-L-prolinamide to treat ischemia reperfusion injury.

The instant invention differs from the cited reference in that the cited reference does not teach the addition of a second agent, a thrombolytic agent as disclosed in claim 26. However, the secondary reference, Verstraete, teaches a thrombolytic agent such as streptokinase to treat myocardial infarction, an ischemia reperfusion injury. Clearly, one skilled in the art would have assumed to combination of two individual agents know to treat ischemia reperfusion injuries into a single composition would give an additive effect in the absence of evidence to the contrary.

The instant invention differs from the cited references in that the cited references do not teach the additional use of a mechanical device for reestablishing blood flow. However, the tertiary reference, Woods, teaches an apparatus used to reestablish blood flow in a patient that involves angioplasty. Clearly, the use of mechanical devices that involves angioplasty is well-known in the art.

Claims 25-28 and 30 are not allowed.

The remaining references listed on the enclosed PTO-892 are cited to show the state of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin E. Weddington whose telephone number is (571)272-0587. The examiner can normally be reached on 11:00 am-7:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kevin E. Weddington
Primary Examiner
Art Unit 1614

K. Weddington
February 20, 2006